



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,673	01/16/2004	Danila Valmori	LUD 5483.7 DIV (10316191)	7395
24972 7590 08/09/2007 FULBRIGHT & JAWORSKI, LLP 666 FIFTH AVE NEW YORK, NY 10103-3198			EXAMINER DIBRINO, MARIANNE NMN	
			ART UNIT 1644	PAPER NUMBER
			MAIL DATE 08/09/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/758,673

Applicant(s)

VALMORI ET AL.

Examiner

DiBrino Marianne

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 19-23 is/are pending in the application.
- 4a) Of the above claim(s) 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 19-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. Applicant's amendment filed 5/23/07 is acknowledged and has been entered.

The Declaration of Inventors Valmori, Cerottini and Romero under 37 CFR 1.132 in view of *In Re Katz* is acknowledged and has been entered.

2. The Terminal Disclaimer filed 5/23/07 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of the full statutory term of prior patent No. 5,662,907 is hereby DISAPPROVED because there are no common owners/inventors with the instant application.

3. Applicant is reminded of Applicant's election of Group I, drawn to a method for inducing proliferation of CTL, said method comprising contacting a sample containing CTLp with a polytope, wherein said polytope comprises an amino acid sequence found in a Melan-A molecule and said sequence forms a complex with an HLA class I molecule, and species of SEQ ID NO: 9 in Applicant's response filed 11/2/06.

Claim 19-22 read on the elected species, SEQ ID NO: 9. As SEQ ID NO: 9 appears to be free of the prior art, the search has been extended to include SEQ ID NO: 6.

Claims 19-22 are presently being examined as they read SEQ ID NO: 6.

4. The disclosure is objected to because of the following informalities:

The font size used for Table V on page 17 and for Table IV of the specification is too small to be read clearly.

Appropriate correction(s) is/are required.

The following is a new ground of rejection necessitated by Applicant's amendment filed 5/23/07.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is indefinite in the recitation of "polytope comprises an amino acid sequence found in a Melan-A molecule, wherein said amino acid sequence forms a complex with an HLA molecule....which process said polytope to Melan-A peptides which complex with said HLA molecules, wherein the complexes of said HLA molecules and Melan-A

Art Unit: 1644

peptides induce proliferation of cytolytic T cells" because it is not clear what is meant, *i.e.*, the polytope comprises an amino acid sequence (one peptide) that forms a complex with an HLA molecule, but the polytope is processed to more than one peptide and those peptides from Melan-A complex with HLA molecules and induce proliferation of CTLs.

7. For the purpose of prior art rejections, the filing date of the instant claims 19-22 is deemed to be the filing date of the 09/061,388 parent application, *i.e.*, 4/16/98, as the 08/880,963 parent application does not support the claimed limitation "polytope" recited in claims 19 and 22 of the instant application.

8. The Declaration of Inventors Valmori, Cerottini and Romero under 37 CFR 1.132 in view of *In Re Katz* filed 5/23/07 has overcome the prior rejection of record based upon Valmori et al (J. Immunol. 160: 1750-1758, 2/98, IDS reference).

The following are new grounds of rejection necessitated by Applicant's amendment and Rule 1.132 Declaration, both filed 5/23/07.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,965,017 B2 in view of Gilbert *et al* (Nature Biotech. 1997, 15: 1280-1284, of record) and US Patent No. 5,662,907 (of record).

US 6,965,017 B2 discloses a Melan-A/MART-1 peptides in Table 14 that may be exposed to lymphocytes and the lymphocytes used for adoptive transfer. US 6,965,017 discloses that the T cells that are stimulated with peptide(s) may be present in a sample comprising PBL (peripheral blood mononuclear cells that contain antigen presenting cells with MHC class I on their surface to which the peptide(s) bind(s)). US 6,965,017 B2 discloses that although some of the peptides listed in Table 14 were not recognized by the particular T cells used in the study, they have higher binding affinity to HLA-A2.1 and may induce a different set of T cells capable of recognizing the original melanoma epitopes *in vitro* or *in vivo*. US 6,965,017 B2 discloses a peptide consisting of AMGIGILTV (identical to SEQ ID NO: 6 of the instant claim 22) that has a high affinity of binding to HLA-A2.1. US 6,965,017 B2 discloses that these peptides may be used for induction of anti-melanoma T cells *in vitro* and immunization of patients for the treatment of melanoma. US 6,965,017 B2 discloses peptide antigens from other melanoma proteins that may be used in conjunction with the Melan-A/MART-1 peptides (especially column 20 at lines 10-22, column 57 at lines 5-44 and abstract).

Art Unit: 1644

US 6,965,017 B2 does not disclose a method of *in vitro* stimulation of T cells with SEQ ID NO: 6 and other Melan-A/MART-1 peptides listed in Table 14 wherein the Melan-A analog peptide(s) is/are in the form of a polytope, nor does US 6,965,017 explicitly disclose that in adoptive therapy CTL the stimulating peptides are added to cells that present HLA molecules on their surface.

Gilbert *et al* teach constructing polytope proteins comprising one or more class I MHC-restricted CTL epitopes and the p1 protein of the retrotransposon Ty1 of *S. cerevisiae*, and optionally also comprising CD4 epitopes. Gilbert *et al* teach that their polytope protein consists of a single protein species that can be simply produced in yeast at high yields and carries a string of up to 15 defined CTL epitopes from *Plasmodium* species, said polytope protein effectively primes protective CTL responses in mice following a single administration without adjuvant. Gilbert *et al* teach that effective processing of epitopes from the string was demonstrated *in vitro* and *in vivo* and was not affected by flanking sequences. Gilbert *et al* teach that using minimal epitopes to produce vaccines instead of whole antigens enables the immune response to be directed towards conserved regions of antigens. Gilbert *et al* teach that in mice, the response towards the polyepitope protein is long lasting and can be boosted, that in humans they are safe and elicit cellular and proliferative responses to the vaccine. Gilbert *et al* teach that in humans, use of alum adjuvant impairs CTL response, but in a phase I trial where no adjuvant was used, CTL responses were induced to the polyepitope protein (see entire article, especially abstract, introduction, discussion).

US Patent No. 5,662,907 discloses contacting CTL with an immunogenic peptide *in vitro* and then reintroducing the activated cells into a patient with cancer, such as melanoma, or that alternatively, the peptides can be used as a vaccine to induce an immune response *in vivo*, or a combination of both methods may be used. US Patent No. 5,662,907 discloses that the peptides may be used therapeutically to elicit CTL responses to melanoma in the form of a peptidic vaccine, or for *ex vivo* therapy in which CTL are induced in tissue culture and used for adoptive immunotherapy. US Patent No. 5,662,907 discloses that *ex vivo* CTL responses to a tumor antigen are induced by incubating in tissue culture the patient's CTL precursor cells together with a source of antigen presenting cells (APC) and the appropriate immunogenic peptide. US Patent No. 5,662,907 discloses using more than one peptide in a vaccine or using heteropolymers of different peptides for stimulating CTL responses for the advantage of increased immunological reaction and the additional ability to induce CTL that react with different antigenic determinant of the tumor cells, and different types of APC, including autologous PBMC, pAPC such as dendritic cells and activated B cells (especially column 2 at lines 26-33, column 4 at lines 8-16, column 12 at lines 13-44, column 13 at lines 19-37).

Art Unit: 1644

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made a vaccine composition containing the Melan-A, MART-1 peptides, such as AMGIGILTV, disclosed by US 6,965,017 in the form of a polypeptide (*i.e.*, polytope) peptide as taught by Gilbert *et al* or as disclosed by US Patent No. 5,662,907, either in combination with other Melan-A analog peptides disclosed by US 6,965,017 or with other melanoma tumor associated antigenic peptides such as those disclosed by US Patent No. 5,662,907 or such as those disclosed by US 6,965,017, and to have used the polytope peptide to stimulate CTLp *in vitro* using APC expressing the HLA-A\*0201 restriction element disclosed by US 6,965,017 or disclosed by US Patent No. 5,662,907 in the method of stimulating CTLp *ex vivo* disclosed by US 6,965,017 or disclosed by US Patent No. 5,662,907.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to expand CTL for adoptive therapy as disclosed by US 6,965,017 and by US Patent No. 5,662,907 as a modality for treating melanoma as disclosed by US Patent No. 5,662,907 or by US 6,965,017, because US 6,965,017 disclose that the Melan-A/MART-1 peptides in Table 14 such as AMGIGILTV may be used for immunizing a patient, both Gilbert *et al* teach and US Patent No. 5,662,907 discloses the advantages of using a polytope vaccine over a single epitope vaccine. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make CTL for the adoptive therapy component of the combination therapy disclosed by US Patent No. 5,662,907 of using both *ex vivo* stimulated CTL and the peptide vaccine, and because US Patent No. 5,662,907 discloses using more than one peptide in a vaccine in the form a heteropolymer of active peptide units for the advantage of an increased immune response and reactivity against more than one antigenic determinant on a tumor cell.

11. Claims 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,844,075 in view of Gilbert *et al* (Nature Biotech. 1997, 15: 1280-1284, of record) and US Patent No. 5,662,907 (of record).

US 5,844,075 discloses a Melan-A/MART-1 peptides in Table 14 that may be exposed to lymphocytes and the lymphocytes used for adoptive transfer. US 5,844,075 discloses that the T cells that are stimulated with peptide(s) may be present in a sample comprising PBL (peripheral blood mononuclear cells that contain antigen presenting cells with MHC class I on their surface to which the peptide(s) bind(s)). US 5,844,075 discloses that although some of the peptides listed in Table 14 were not recognized by the particular T cells used in the study, they have higher binding affinity to HLA-A2.1 and may induce a different set of T cells capable of recognizing the original melanoma epitopes *in vitro* or *in vivo*. US 5,844,075 discloses a peptide consisting of AMGIGILTV (identical to SEQ ID NO: 6 of the instant claim 22) that has a high affinity of binding to HLA-A2.1. US 5,844,075 discloses that these peptides may be used for induction of anti-melanoma T cells *in vitro* and immunization of patients for the treatment of melanoma. US 5,844,075 discloses peptide antigens from other melanoma proteins

Art Unit: 1644

that may be used in conjunction with the Melan-A/MART-1 peptides (especially paragraph spanning columns 19-20, paragraph spanning columns 55-56, column 56 at lines 6-44, and abstract).

US 5,844,075 does not disclose a method of *in vitro* stimulation of T cells with SEQ ID NO: 6 and other Melan-A/MART-1 peptides listed in Table 14 wherein the Melan-A analog peptide(s) is/are in the form of a polytope, nor does US 6,965,017 explicitly disclose that in adoptive therapy CTL the stimulating peptides are added to cells that present HLA molecules on their surface.

Gilbert *et al* teach constructing polytope proteins comprising one or more class I MHC-restricted CTL epitopes and the p1 protein of the retrotransposon Ty1 of *S. cerevisiae*, and optionally also comprising CD4 epitopes. Gilbert *et al* teach that their polytope protein consists of a single protein species that can be simply produced in yeast at high yields and carries a string of up to 15 defined CTL epitopes from *Plasmodium* species, said polytope protein effectively primes protective CTL responses in mice following a single administration without adjuvant. Gilbert *et al* teach that effective processing of epitopes from the string was demonstrated *in vitro* and *in vivo* and was not affected by flanking sequences. Gilbert *et al* teach that using minimal epitopes to produce vaccines instead of whole antigens enables the immune response to be directed towards conserved regions of antigens. Gilbert *et al* teach that in mice, the response towards the polyepitope protein is long lasting and can be boosted, that in humans they are safe and elicit cellular and proliferative responses to the vaccine. Gilbert *et al* teach that in humans, use of alum adjuvant impairs CTL response, but in a phase I trial where no adjuvant was used, CTL responses were induced to the polyepitope protein (see entire article, especially abstract, introduction, discussion).

US Patent No. 5,662,907 discloses contacting CTL with an immunogenic peptide *in vitro* and then reintroducing the activated cells into a patient with cancer, such as melanoma, or that alternatively, the peptides can be used as a vaccine to induce an immune response *in vivo*, or a combination of both methods may be used. US Patent No. 5,662,907 discloses that the peptides may be used therapeutically to elicit CTL responses to melanoma in the form of a peptidic vaccine, or for *ex vivo* therapy in which CTL are induced in tissue culture and used for adoptive immunotherapy. US Patent No. 5,662,907 discloses that *ex vivo* CTL responses to a tumor antigen are induced by incubating in tissue culture the patient's CTL precursor cells together with a source of antigen presenting cells (APC) and the appropriate immunogenic peptide. US Patent No. 5,662,907 discloses using more than one peptide in a vaccine or using heteropolymers of different peptides for stimulating CTL responses for the advantage of increased immunological reaction and the additional ability to induce CTL that react with different antigenic determinant of the tumor cells, and different types of APC, including autologous PBMC, pAPC such as dendritic cells and activated B cells (especially column 2 at lines 26-33, column 4 at lines 8-16, column 12 at lines 13-44, column 13 at lines 19-37).

Art Unit: 1644

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made a vaccine composition containing the Melan-A, MART-1 peptides, such as AMGIGILTV, disclosed by US 5,844,075 in the form of a polypeptide (*i.e.*, polytope) peptide as taught by Gilbert *et al* or as disclosed by US Patent No. 5,662,907, either in combination with other Melan-A analog peptides disclosed by US 5,844,075 or with other melanoma tumor associated antigenic peptides such as those disclosed by US Patent No. 5,662,907 or such as those disclosed by US 6,965,017, and to have used the polytope peptide to stimulate CTLp *in vitro* using APC expressing the HLA-A\*0201 restriction element disclosed by US 6,965,017 or disclosed by US Patent No. 5,662,907 in the method of stimulating CTL *ex vivo* disclosed by US 5,844,075 or disclosed by US Patent No. 5,662,907.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to expand CTL for adoptive therapy as disclosed by US 5,844,075 and by US Patent No. 5,662,907 as a modality for treating melanoma as disclosed by US Patent No. 5,662,907 or by US 5,844,075, because US 6,965,017 disclose that the Melan-A/MART-1 peptides in Table 14 such as AMGIGILTV may be used for immunizing a patient, both Gilbert *et al* teach and US Patent No. 5,662,907 discloses the advantages of using a polytope vaccine over a single epitope vaccine. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make CTL for the adoptive therapy component of the combination therapy disclosed by US Patent No. 5,662,907 of using both *ex vivo* stimulated CTL and the peptide vaccine, and because US Patent No. 5,662,907 discloses using more than one peptide in a vaccine in the form a heteropolymer of active peptide units for the advantage of an increased immune response and reactivity against more than one antigenic determinant on a tumor cell.

The following ground of rejection remains.

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).



Art Unit: 1644

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 19-22 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,326,200 in view of Gilbert *et al* (Nature Biotech. 1997, 15: 1280-1284) and US Patent No. 5,662,907.

Claims 1-4 of U.S. Patent No. 6,326,200 recite a method for provoking proliferation of CTL comprising contacting a sample containing CTLp with a complex of a peptide and an HLA-A2 molecule, wherein the sequence of the peptide is an amino acid sequence found in Melan-A that is one of SEQ ID NO: 13-15 (that are identical to SEQ ID NO: 13-15 recited in instant claim 22).

Claims 1-4 of U.S. Patent No. 6,326,200 do not recite that the method comprises contacting the CTLp with a polytope, wherein said polytope comprises an amino acid sequence found in Melan-A, including SEQ ID NO: 13-15 recited in instant claim 22, and a sample of cells which present HLA molecules on their surfaces and which process said polytope to Melan-A peptides that complex with said HLA molecules, including wherein the HLA molecule is HLA-A2 recited in instant claim 21.

Gilbert *et al* teach constructing polytope proteins comprising one or more class I MHC-restricted CTL epitopes and the p1 protein of the retrotransposon Ty1 of *S. cerevisiae*, and optionally also comprising CD4 epitopes. Gilbert *et al* teach that their polytope protein consists of a single protein species that can be simply produced in yeast at high yields and carries a string of up to 15 defined CTL epitopes from *Plasmodium* species, said polytope protein effectively primes protective CTL responses in mice following a single administration without adjuvant. Gilbert *et al* teach that effective processing of epitopes from the string was demonstrated *in vitro* and *in vivo* and was not affected by flanking sequences. Gilbert *et al* teach that using minimal epitopes to produce vaccines instead of whole antigens enables the immune response to be directed towards conserved regions of antigens. Gilbert *et al* teach that in mice, the response towards the polyepitope protein is long lasting and can be boosted, that in humans they are safe and elicit cellular and proliferative responses to the vaccine. Gilbert *et al* teach that in humans, use of alum adjuvant impairs CTL response, but in a phase I trial where no adjuvant was used, CTL responses were induced to the polyepitope protein (see entire article, especially abstract, introduction, discussion).

Art Unit: 1644

US Patent No. 5,662,907 discloses contacting CTL with an immunogenic peptide *in vitro* and then reintroducing the activated cells into a patient with cancer, such as melanoma, or that alternatively, the peptides can be used as a vaccine to induce an immune response *in vivo*, or a combination of both methods may be used. US Patent No. 5,662,907 discloses that the peptides may be used therapeutically to elicit CTL responses to melanoma in the form of a peptidic vaccine, or for *ex vivo* therapy in which CTL are induced in tissue culture and used for adoptive immunotherapy. US Patent No. 5,662,907 discloses that *ex vivo* CTL responses to a tumor antigen are induced by incubating in tissue culture the patient's CTL precursor cells together with a source of antigen presenting cells (APC) and the appropriate immunogenic peptide. US Patent No. 5,662,907 discloses using more than one peptide in a vaccine or using heteropolymers of different peptides for stimulating CTL responses for the advantage of increased immunological reaction and the additional ability to induce CTL that react with different antigenic determinant of the tumor cells, and different types of APC, including autologous PBMC, pAPC such as dendritic cells and activated B cells (especially column 2 at lines 26-33, column 4 at lines 8-16, column 12 at lines 13-44, column 13 at lines 19-37).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have made and used a polytope such as taught by Gilbert *et al* and disclosed by US Patent No. 5,662,907 in the method of claims 1-4 of '200, *i.e.*, to have made a complex of the peptide and HLA-A2 using a polytope peptide that would be processed to form the said complex.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate CTLp *ex vivo* as disclosed by US Patent No. 5,662,907 using a polyepitope peptide with multiple CTL epitopes taught by both references to be advantageous in increased immune response with multiple CTL specificities to tumor antigens, and for generating CTL *ex vivo* for adoptive immunotherapy or the combination therapy disclosed by US Patent No. 5,662,907.

Applicant's arguments of record on page 7 in the amendment filed 5/23/07 have been fully considered, but are not persuasive.

It is the Examiner's position that the terminal disclaimer to US 6,552,907 is disapproved as enunciated at item #2 of this Office Action because there are no inventors or owners in common with the instant application.

14. No claim is allowed.

Art Unit: 1644


15. Applicant's amendment and Declaration under Rule 1.132 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.


16. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Marianne DiBrino, Ph.D.  
Patent Examiner  
Group 1640  
Technology Center 1600  
July 27, 2007



CHRISTINA CHAN  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600